

Severe Gangrene of the Stomach and Infarction of the Liver and Spleen After Percutaneous Ethanol Injection for Hepatocellular Carcinoma : Report of a Case

Kuo-Chih Tseng, Shao-Jer Chen¹, An-Liang Chou, Jeh-En Tzeng²,
Hong-Ming Tsai³, and Pin-Nan Cheng⁴

Department of Internal Medicine, ¹Radiology, ²Pathology, Buddhist Dalin Tzu Chi General Hospital, Chiayi, Taiwan; ³Departments of Radiology, ⁴Internal Medicine, National Cheng Kung University Hospital, Tainan, Taiwan

Abstract

Percutaneous ethanol injection is a safe and effective treatment for small hepatocellular carcinoma. The complication rate is lower in the injury of liver, stomach and spleen. We herein report an 82-year-old female with chronic hepatitis C-related hepatocellular carcinoma, measuring 4.0 x 2.8 cm in the left lobe of liver. Because of high risk of surgery, she received percutaneous ethanol injection in segmental fractions with 1-2 cc in one fraction, total 20 milliliter of 95% ethanol in one session, and then soon suffered complications of gangrene of the stomach and infarction of the liver and spleen. Although surgical intervention and intensive care were administrated, she finally died of sepsis with multiple organ failure. The mechanism of percutaneous ethanol injection-related injuries to a combination of stomach, liver and spleen is probably vascular injury by ethanol. It is recommended that a slower injection speed, small amounts of ethanol during procedure and assessment of vascular anatomy before percutaneous ethanol injection are needed to avoid such severe ethanol-induced vessel injury. (J Intern Med Taiwan 2006; 17: 33-38)

Key Words : Hepatocellular carcinoma, Percutaneous ethanol injection, Gangrene, infarction.

Introduction

Hepatocellular carcinoma (HCC) is one of the most common malignancies in the world and the leading cause of cancer deaths in Taiwan. In addition to surgery and transcatheter arterial embolization (TAE), percutaneous ethanol injection (PEI) has been widely used for patients with HCC, especially for patients with a single HCC nodule whose diameter is less than five centimeters, or with less than three tumor foci, the largest being less than three centimeters¹⁻³. The technique is considered to be safe with a lower complication rate, ranging from 1.3% to 3.2%, which can be managed conservatively^{1,3}. Only one possible fatal complication has been published due to liver necrosis after PEI⁴. Recently, there were two reports of PEI associated gastric injuries, supposedly resulting from vessel injury induced by ethanol^{5,6}. We here report a case with severe complications in the liver, stomach and spleen after PEI for HCC.

Case Report

An 82-year-old female patient had chronic hepa-

titis C and hypertension under medical treatment for several years. She received regular follow-up examinations at a clinic, and a hepatic tumor was diagnosed in Feb 2001. She was then admitted to National Cheng Kung University Hospital in Taiwan for further evaluation and management. During admission, physical examination revealed temperature, 36.8 °C; pulse rate, 56/min; respiratory rate, 16/min; blood pressure, 141/93 mmHg. Neither stigmata of cirrhosis nor palpable lymph nodes were found. Laboratory investigations disclosed white blood count of 7100/mm³ (normal range: 3200-9200/mm³); hemoglobin of 12.7 g/dl (11.6-14.8 g/dl); platelet count of 232000/mm³ (138000-353000/mm³); prothrombin time of 12.1 sec (10.5-13.5 sec); aspartate aminotransferase (AST) of 35 IU/L (5-40 IU/L); alanine aminotransferase (ALT) of 32 IU/L (5-55 IU/L); total bilirubin of 0.4 mg/dl (0.2-1.4 mg/dl); albumin of 3.7 g/dl (3.0-5.0 g/dl); alfa-fetoprotein of 5.8 ng/ml (< 20 ng/ml). Abdominal sonography and enhanced computed tomography scan showed a hepatic tumor, located in segment II of the liver, measuring about 4.0 x 2.8 centimeters in size. Liver biopsy was performed on the

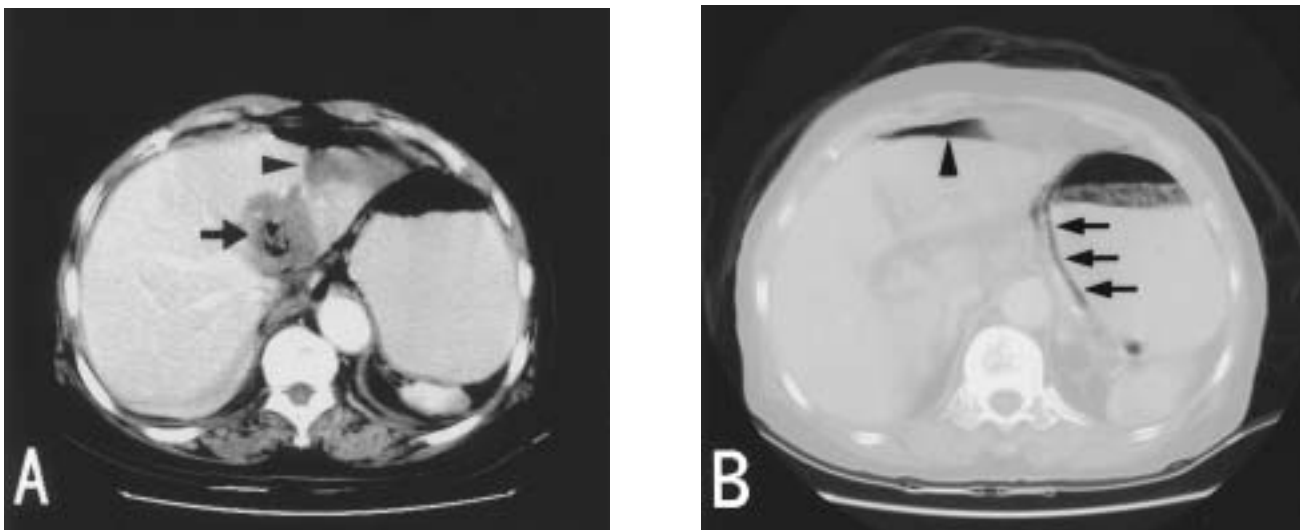


Fig. 1A. The enhanced computed tomography demonstrated that the injection site of ethanol became a poorly enhanced area with central air collection (arrow) and another wedge-shaped area distally (arrowhead), which implies ethanol-induced infarction of the liver.

B. In the lung window display, a transmurial air-content layer was noted in the lesser curvature site of the stomach over the left gastric artery territory after PEI, implying the gangrene change of the stomach (arrow). Intraperitoneal air was also found around the anterior surface of the left lobe of the liver (arrowhead).

second day of admission and the pathology disclosed well-differentiated HCC. Considering the high risk for operation, PEI was conducted with 20 milliliter (ml) of 95 % ethanol injected to HCC in segment II under real-time sonographic guidance on the third day of admission. The course was smooth and the ethanol was injected in segmental fractions with 1-2 cc in one fraction. Several hours after ethanol injection, persistent epigastric pain was noted. The pain was exacerbated on the second day after PEI administration, and was associated with fever and shortness of breath. The plain film of abdomen showed marked ileus. Emergent computed tomography scan demonstrated infarction of the left lobe of the liver (Fig. 1A), gangrene change in the lesser curvature of the stomach, and intraperitoneal air (Fig. 1B). PEI related vessel injury was suspected. Because of her deteriorating

condition, she received emergency operation on the same day. The operative finding revealed diffuse erythema with patches of necrosis of the left lobe liver, gangrene change from the angle to the high body of lesser curvature, and splenic infarction. Proximal hemigastrectomy, esophagogastrotomy and splenectomy were performed. The pathology of surgical specimen disclosed infarction and inflammation of the mucosal and submucosal layers, necrosis with pneumatocoles of the muscular layer of stomach (Fig. 2A and 2B) and infarction of the spleen. The condition after operation was unstable and grave, with infections of enterococcus and fungus, multiple organ failure with disseminated intravascular coagulation, acute renal failure, and acute respiratory failure. Although intensive treatment was administrated, the patient died on the 15th day after PEI.

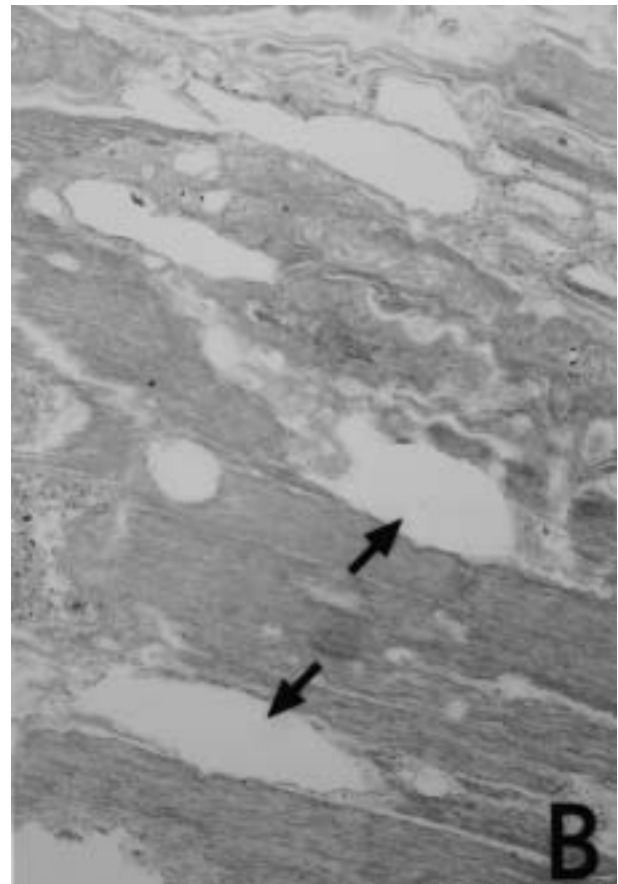
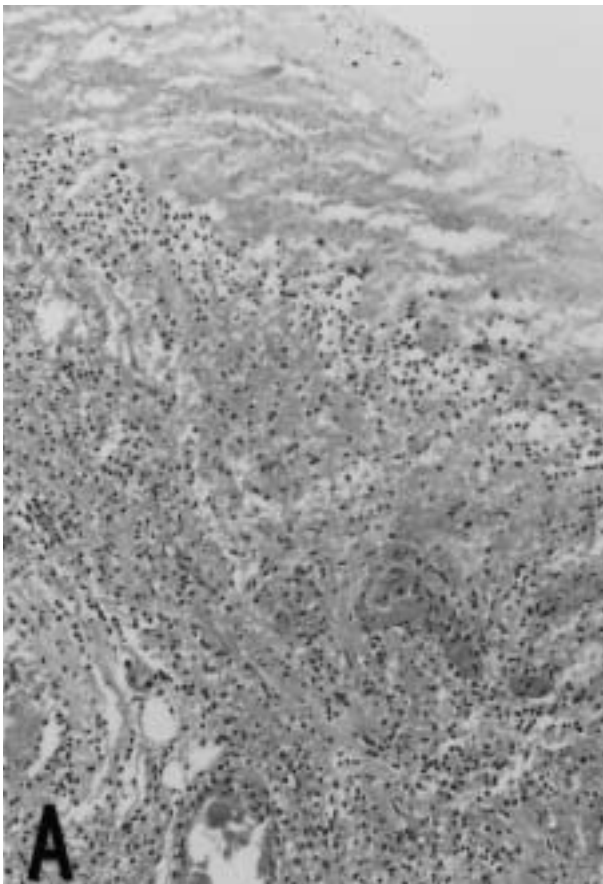


Fig.2A.The pathology showed hemorrhagic infarct in the mucosal layer and acute inflammation and congestion in the submucosal layer. (H&E 100X)

B.In the muscular layer, extensive myonecrosis was noted with pneumatocoles (arrow). (H&E 200X)

Discussion

HCC is one of the most common malignant neoplasms worldwide, especially in endemic areas of chronic hepatitis B or C⁷. It has been the leading cause of mortality of malignancies in Taiwan for many decades. Several treatment modalities have been used for HCC, including surgery, TAE, PEI and radiofrequency ablation. PEI can improve a patient's survival and is as effective as surgery for small solitary HCC^{1,2}. Combination therapy with TAE and PEI is also effective for patients with large HCC and cirrhosis⁸.

The complications of PEI are usually mild, which include fever, abdominal pain and impaired liver function. These manifestations are transient and usually disappear within one week. A few adverse effects have been reported, including peritoneal hemorrhage^{1,2,9}, hemobilia^{1,10}, liver abscess^{1,11}, thrombosis of portal vein branch^{8,12}, needle tract seeding^{13,14}, and hepatic infarction¹⁵. In spite of diverse complication, the generalized major complication rate is around 1.3% to 3.2%^{1,3}. Very few fatalities were reported. Livraghi et al. reported a patient who died of esophageal varices bleeding five days after PEI. But the relationship remained uncertain¹. Taavitsainen et al. reported another mortality that was probably owing to liver necrosis after PEI⁴.

For our patient, mortality was derived from gangrene of the stomach and infarction of the liver and spleen, inducing sequential multiple organ failure. The probable mechanism is organ associated vessel injury by injected ethanol. In addition to that normally derived from left hepatic artery which arising from celiac trunk, the blood supply of left lobe also came from the left hepatic artery of the left gastric artery, or an accessory left hepatic artery of the left gastric artery. The incidence of such normal variant was about 18% reported by Chuang et al. series¹⁶. Gastric injury such as severe gastric mucosal injury and gastric ulcer were reported^{5,6}. The proposed

mechanism underlying these injuries may be associated with the reflux of pure ethanol into the left gastric artery. In our patient, in addition to gangrene of the stomach, the infarction of the liver and spleen was related to the similar mechanism, namely, reflux of ethanol causing the injury to the left gastric artery and the splenic artery.

The amount of ethanol and the speed of injection during PEI possibly contributed to the severe complications in our patient. Generally speaking, small amounts of pure ethanol in each session, usually less than 8 ml, are recommended². However, for large HCC, more sessions of pure ethanol injection are required to achieve therapeutic effect and were reported to increase the possibility of tumor seeding¹⁴. With regard to the safety of high-dose pure ethanol injection in one session during procedure of PEI, neither serious adverse effects nor dose-related major complications were reported^{17,18}. The authors concluded the use of higher amounts of ethanol is acceptable. Besides, the amounts of ethanol in two case reports causing gastric injury were less than 5ml and suggested that the amount of ethanol is possible, but not the only factor associated with vessel injury^{5,6}. For the speed of ethanol injection, most studies suggested a slower rate with 1 ml in 5-10 seconds to avoid complications¹⁸. Rapid injection will increase the opportunity of reflux of ethanol into the vessels.

In conclusion, this is a rare case of severe gangrene of the stomach and infarction of the liver and spleen after PEI for HCC. Although PEI is a safe and effective procedure for HCC, it is worthy to note that a slower injection speed, small amounts of ethanol during procedure and assessment of vascular anatomy before PEI are needed to avoid such ethanol-induced vessel injury.

References

1. Livraghi T, Giorgio A, Marin G, et al. Hepatocellular carcinoma and cirrhosis in 746 patients: long-term results of percutaneous ethanol injection. *Radiology* 1995; 197: 101-8.
2. Shiina S, Tagawa K, Niwa Y, et al. Percutaneous ethanol injection

- tion therapy for hepatocellular carcinoma: results in 146 patients. *Am J Roentgenol* 1993; 160: 1023-8.
3. Di Stasi M, Buscarini L, Livraghi T, et al. Percutaneous ethanol injection in the treatment of hepatocellular carcinoma: a multi-center survey of evaluation practices and complication rates. *Scand J Gastroenterol* 1997; 32: 1168-73.
 4. Taavitsainen M, Vehmas T, Kauppila R: Fatal liver necrosis following percutaneous ethanol injection for hepatocellular carcinoma. *Abdom Imaging* 1993; 18: 357-9.
 5. Su YC, Lu SN, Wu DC, et al. Severe gastric mucosa injury after percutaneous pure ethanol injection therapy for hepatocellular carcinoma. *Gastrointest Endosc* 2000; 51: 350-3.
 6. Seki S, Kitada T, Otagawa K, et al. Gastric ulcer as a rare complication of percutaneous ethanol injection for hepatocellular carcinoma. *Am J Gastroenterol* 2002; 97: 770-1.
 7. Chen CY, Yu MW, Liaw YF: Epidemiological characteristics and risk factors of hepatocellular carcinoma. *J Gastroenterol Hepatol* 1997; 12: S294-308.
 8. Tanaka K, Nakamura S, Numata K, et al. The long term efficacy of combined transcatheter arterial embolization and percutaneous ethanol injection in the treatment of patients with large hepatocellular carcinoma and cirrhosis. *Cancer* 1998; 82: 78-85.
 9. Ohmoto K, Kunieda T, Shibata N, et al. Intraoperative hemorrhage as a major complication of percutaneous ethanol injection therapy for hepatocellular carcinoma. *Hepato-Gastroenterol* 2000; 47: 1199-202.
 10. De Sio I, Castellano L, Calandra M: Hemobilia following percutaneous ethanol injection for hepatocellular carcinoma in a cirrhotic patient. *J Clin Ultrasound* 1992; 20: 621-3.
 11. Isobe H, Fukai T, Iwamoto H, et al. Liver abscess complicating intratumoral ethanol injection therapy for HCC. *Am J Gastroenterol* 1990; 85: 1646-8.
 12. Lencioni R, Cioni D, Uliana M, et al. Fatal thrombosis of the portal vein following single-session percutaneous ethanol injection therapy for hepatocellular carcinoma. *Abdom imaging* 1998; 23: 608-10.
 13. Ishii H, Okada S, Okusaka T, et al. Needle tract implantation of hepatocellular carcinoma after percutaneous ethanol injection. *Cancer* 1998; 82: 1638-42.
 14. Cedrone A, Rapaccini GL, Pompili M, et al. Neoplastic seeding complicating percutaneous ethanol injection for the treatment of hepatocellular carcinoma. *Radiology* 1992; 183: 787-8.
 15. Seki T, Wakabayashi M, Nakagawa T, et al. Hepatic infarction following percutaneous ethanol injection therapy for hepatocellular carcinoma. *Eur J Gastroenterol Hepatol* 1998; 10: 915-8.
 16. Chuang VP, Wallace S: Hepatic arterial redistribution for intraarterial infusion of hepatic neoplasms. *Radiology* 1980; 135: 295-9.
 17. Redvanly RD, Chezmar JL, Strauss RM, et al. Malignant hepatic tumors: safety of high-dose percutaneous ethanol ablation therapy. *Radiology* 1993; 188: 283-5.
 18. Livraghi T, Benedini V, Lazzaroni S, et al. Long term results of single session percutaneous ethanol injection in patients with large hepatocellular carcinoma. *Cancer* 1998; 83: 48-57.

肝癌病人經酒精注射治療後引起嚴重之胃壞疽及 肝脾梗塞：一病例報告

曾國枝 陳紹哲¹ 周安良 曾志恩² 蔡宏名³ 鄭斌男⁴

佛教大林慈濟綜合醫院 內科¹ 放射科² 病理科

國立成功大學附設醫院³ 放射科⁴ 內科

摘 要

酒精注射治療對小型肝癌是一安全及有效之治療方式。其引起對肝脾及胃之併發症的比例極低。本病例報告為一82歲慢性C型肝炎女性，在肝臟左葉產生一4.0x2.8公分之肝腫瘤，經切片診斷為肝癌。因開刀的高危險性，她接受酒精注射治療，方式為分段注射1-2毫升95%酒精，單次共20毫升。之後產生嚴重之胃壞疽及肝脾梗塞的併發症。儘管立即開刀並給予積極治療，該病患還是因敗血症併多重器官衰竭往生。本篇將探討其引發肝脾及胃併發症可能之機轉。一般建議當執行肝癌酒精注射治療時，速度慢、小劑量及術前評估血管行路變異為避免如此嚴重之併發症之方法。